sufficient to indicate that the proposal for widespread amendments to medical practice acts is neither simple nor devoid of danger to medical standards.

For the information of members of the California Medical Association, it may be stated that the members of the C.M.A. Council gave the subject of amendments to the State's Medical Practice Act careful consideration. The conclusion was reached that certain simple amendments, suggested by the Board of Medical Examiners would make it possible for that Board to meet any emergencies that might arise. The proposed amendments will make for simpler procedures in giving examinations, which also may be more frequently held. It is believed these will answer medical service needs, and without endangering California's established standards.

California's 55th Legislature in Recess during February: Proposed Legislation.—This year, under existing war conditions, even the California Legislature is holding what may be called a modified, streamlined gathering. The 55th session convened on Monday, January 4th and by the constitution could remain in session for not exceeding thirty days; then to recess for not more than thirty days. The Legislature is booked to reconvene on Monday, March 8th.

At this writing, it is not possible to present to readers a complete list of all proposed legislation having direct or indirect relationship to public health and medical matters and standards. A partial list appears in this issue on page 79. The committees on public policy and legislation of the county medical societies should scan the above lists and also any others that may be sent.

In the January number, on pages 35 and 36, the rosters of the two legislative houses were printed, the home addresses of State Senators and Assemblymen being given. It may be desirable to preserve the lists for future use and reference. (A summary on legislation of medical interest, presented to the U. S. Congress in the year 1942, appears on page 74 of this number of CALIFORNIA AND WESTERN MEDICINE.)

It is too early to state with positiveness what struggles may come to the front on legislation in which medicine and the associated professions have natural interests. When the 55th Legislature again convenes on March 8th, the legislators will take up in earnest the consideration of proposed laws. Fortunately, the medical profession does not have before it, a menace such as confronted it some four years ago, when the then Governor espoused a Compulsory Health Act as an item of "must legislation," that was to be enacted forthwith, willy nilly. For the defeat of that project, physicians of California may continue to render thanks.

In due course, bulletins will be sent to the component county societies, informing them concerning the more pertinent matters, and indicating procedures on appropriate lines of desirable action. In the meantime it will be wise procedure if county societies, their officers and committees, and also members, refrain from giving endorsements to proposed legislation, except as such may be requested by the C.M.A. Committee on Public Policy and Legislation of which Doctor Dwight Murray of Napa, is chairman. This in accord with past action of the C.M.A. House of Delegates. (For Committee roster, see adv. page 2.)

EDITORIAL COMMENT†

OSTEOPATHIC AND CHIROPRACTIC IMMUNOLOGY

Experimental evidence of the nonexistence of the alleged "immunity center" in the brain, the theoretical basis of much of osteopathic and chiropractic therapy, is currently reported by Stanton[1] and his coworkers of the New York State Psychiatric Institute.

The first serious suggestion of a neurological integration of specific immunity came from a study of the effects of certain drugs on serum titer. Some of these drugs were known or assumed to act primarily on the central or peripheral nervous system. Both increases and decreases of specific antibody production were reported, sufficient to make plausible the existence of a specific "immunity center" in the brain.

Metalnikov,[2] and Diacono,[3] and others attempted to confirm this plausibility by a study of immunologic conditioned reflexes. Animals were given an electric shock or other conditioning stimulus immediately before injection of heat-killed bacterial vaccines or alien erythrocytes. After numerous repetitions of this association, the rabbits showed a significant rise in homologous antibody titer on application of the conditioning stimulus alone. Few if any controls were tested. Using a large number of animals with adequate controls, Kopeloff[4] and his colleagues were unable to confirm these findings. In their hands fluctuations in agglutinin nitrogen were almost identical in conditioned and normal control animals.

Other investigators attempted to confirm the neurogenic origin of specific antibodies by "antigen depot" experiments. Schamburow,[5] for example, injected nonviable typhoid vaccine into the anterior chamber of the rabbit eye. He found the specific agglutinin titer of the aqueous humor of the injected eye increased to 8-fold that of the synchronous agglutinin titer of the blood stream. This he accepted as proof of a local synthesis of specific agglutinins in the injected eye. Studying the opposite, nonvaccinated eye, he often found

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† This department of CALIFORNIA AND WESTERN MEDICINE presents editorial comments by contributing members on items of medical progress, science and practice, and on topics from recent medical books or journals. An invitation is extended to all members of the California Medical Association to submit brief editorial discussions suitable for publication in this department. No presentation should be over five hundred words in length.

an agglutinin titer 2 to 3 times that of the blood stream, conclusive evidence from his point of view of a reflex local synthesis of specific typhoid agglutinins in the nonvaccinated eye. This he believed could only be brought about through a specific "immunity center" in the brain. The experimental data for this conclusion, however, could not be confirmed by Madison[6] and other American investigators.

In contrast with these contradictory results, experiments involving destruction of certain parts of the nervous system have given consistent data. Metalnikov,[4] for example, found that specific anticholera immunity could be produced in certain caterpillars by the injection of heat-killed cholera vaccine. Destruction of the third thoracic ganglion in these caterpillars, however, prevented the development of this specific immunity, destruction of other ganglia having little or no inhibiting effect. Bogendörfer[7] sectioned the spinal cord of dogs usually at the 6th cervical vertebra, control animals being sectioned in the lower thoracic region. All control (low spinal section) animals produced specific agglutinins on injection with bacterial vaccines. Practically no agglutinins were formed by the high-level (cervical) spinal-section dogs. This clearly suggested to him the existence of a neurogenic immunity center, interrupted by high-level spinal cord section.

Stanton and his coworkers attempted to confirm this high-level immunologic paralysis, using white rats as the experimental animals. Rats were selected because of negligible mortality with adequate postoperative care. Groups of from 10 to 20 rats were sectioned between the 1st and 2nd thoracic vertebrae. An equal number of "operated controls" were sectioned between the 6th and 10th thoracic vertebrae. The animals were placed in a warm-box until recovery from the operation. Five to 14 days after recovery both groups, together with an equal number of "nonoperated controls," were given an intraabdominal or intravenous injection of a standard dose of washed sheep erythrocytes. The animals were bled 7 days later, and the antisheep hemolytic titer of each animal estimated with the aid of guinea-pig complement. In a typical experiment, 23 out of a group of 28 nonoperated controls yielded serums with amboceptor titers often as high as 1:2560. Ten of the 13 low-level "operated controls" yielded antiserums with a maximum titer of 1:1280. Among the 19 animals with high thoracic cord section, 15 produced no demonstrable hemolysin. The remaining four gave traces of hemolysin (average titer 1:60). A similar almost complete suppression of specific antibody formation was recorded for all other high-level operated groups, seeming confirmation of the neurogenic theory of specific immunity.

Stanton and his colleagues, however, took cognizance of the fact that the observed "immunologic paralysis" is not the only effect of high-level spinal cord section. The high-level operated animals also lost their normal temperature control. Maintained at ordinary room temperature, their rectal temperatures often fell from the average normal of 34.5 C to 27 C or even lower. Before the existence of a specific "immunologic paralysis" could be deduced from their data, therefore, the possible deleterious effects of this subnormal body-temperature must be ruled out. To do this, parallel groups of high-level spinal cord sectioned rats were maintained at higher external temperatures. At 33 C external temperature the animals showed practically no fall in normal rectal temperature. In these animals antibody production was equal to that of the unoperated controls. This is conclusive evidence that high-level cord section in itself has no deleterious effect on specific antibody synthesis, the observed suppression of immunologic function being a secondary effect of subnormal body-temperature.

Fifty years ago, before the development of modern theories of humoral immunity, Sawtschenko[8] made a similar observation. He found that when the cervical cord was sectioned in pigeons, the birds lost their natural immunity to anthrax. This he attributed to their lowered body-temperature, avian resistance to anthrax then being attributed solely to their high normal body-temperature.

The alleged totalitarian "immunity center" in the brain initiating and coördinating specific antibody production has been of philosophic interest among European investigators largely on account of its political implications.[9] American clinicians, however, will probably find their main interest in its application to certain unofficial methods of clinical therapy. Hulburt,[10] of the American Osteopathic Association, for example, states that it is a basic tenet of osteopathic therapy that interference with spinal function causes "a resulting intemperance with the body's ability to make its own serum and antitoxins to fight infectious disease processes." This theory is endorsed in somewhat more picturesque language by Chiropractors,[11] who allege that as a result of spinal cord injury "the efferent nerves are prevented from transmitting to the various bodily organs the mental impulses necessary for their proper function (e.g., specific antibody production)." Disproof of the neurogenic theory of specific antibody production is, therefore, equivalent to disproof of one of the major basic tenets of both Osteopathy and Chiropractic.

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DIANTIGENIC INSULIN

An apparent confirmation of the newer theories of specific antibody production is seen in the clinical evidence of the existence of two distinct antibodies against crystalline insulin, recently reported by Lowell[1] of the Massachusetts Memorial Hospital.

The earlier immunologists assumed a one-to-one relationship between specific antigen and antibody, all observed allergic or immune phenomena being explained on this basis. The possibility that a single antigen may give rise to two or more different antibodies, however, would follow logically from the more recent template theory of specific antibody synthesis. According to this theory[2] specific antibodies are new-formed protein molecules synthesized intracellularly as "templates" of the injected antigen. Assuming that the antigen is asymmetrical in chemical structure, two or more different templates might be formed to fit its different poles. Moreover, homologous templates formed by different histological units might well be of different structure or function.

One of the best illustrations of the template theory is the recent demonstration by Smadel[3] and his coworkers of the Rockefeller Institute of the dual antigenicity of vaccine elementary bodies. Earlier investigators demonstrated the existence of two different soluble antigens in vaccine lymph,[4] a heat-labile (L) antigenic molecule, readily destroyed by heating to 56° C, and a heat-stable (S) molecule resisting heat to 95° C. There was suggestive evidence that in the elementary bodies the two antigens may be conjugated to form a single protein complex, a duplex LS-antigen capable of reacting equally well with anti-L and anti-S serum. The Rockefeller Institute biochemists isolated this hypothetical LS-complex from dermal pulp of cutaneously infected rabbits, and showed that it is a homogeneous protein of approximately the same molecular size as serum globulin. This protein is precipitated quantitatively with either anti-L or anti-S precipitin. They found that the L-pole of this native antigen can be partially (L') or completely (L") denatured by heat, without demonstrable alteration of the S-pole. By means of enzymic digestion the S-pole can be similarly degraded (S', S") without demonstrable injury to the L-pole. Dissociation of the LS-molecule into free L- and S-proteins, however, was not demonstrated.

The existence of diantigenic proteins affords a convenient explanation of numerous puzzling clinical phenomena. In 1929, for example, Cook and Spain[5] pointed out the lack of correlation between the skin-sensitizing and smooth-muscle sensitizing antibodies formed against the same alien protein. Somewhat later Loveless[6] demonstrated the existence of two antibodies against the same pollens. One of these was a thermostable, nonsensitizing antibody capable of binding pollen-protein, the other a thermolabile, sensitizing antibody presumably responsible for the observed allergic phenomena. Since ragweed pollen is known to be a complex protein mixture, no definite conclusion could be drawn from the observed apparent diantigenicity.

A year ago Yasuna,[7] of the Boston City Hospital, found 11 recorded cases of general sensitivity to crystalline insulin, adequately confirmed by allergy studies. A twelfth case was reported from his Diabetic Clinic, in which severe insulin allergy was associated with marked insulin tolerance. Mouse-test showed that 0.5 c.c. of the patient's serum would neutralize twice the convulsive dose of crystalline insulin. The neutralizing properties were not destroyed by heating the serum to 57° C for 2 hours. A 1:32 dilution of the same serum would passively sensitize normal human skin to crystalline insulin. The skin-sensitizing activity, however, was completely destroyed by heating the serum to 57° C for 2 hours. Lowell concludes from these and other data that "there were two antibodies in the patient's serum, an allergic antibody which is heat-labile and confers sensitivity on normal skin, and an insulin-neutralizing antibody which is heat-stable and was capable of destroying the physiological effects of crystalline insulin."

Insofar as crystalline insulin is a single protein molecule, it would seem logical to conclude that insulin protein is diantigenic, capable of stimulating the production of two functionally distinct antibodies. Insulin would thus be the latest addition to the rapidly increasing list of multiantigenic proteins of theoretical and practical interest. Other explanations of the dual antibodies (anti-insulins) are of course possible.

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